

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A transdermal drug delivery composition ~~consisting of~~ comprising  
(a) a copolymer comprising
  - (i) one or more A monomers selected from the group consisting of alkyl acrylates containing 4 to 12 carbon atoms in the alkyl group and alkyl methacrylates containing 4 to 12 carbon atoms in the alkyl group; and
  - (ii) one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; and  
(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition;  
wherein the composition is substantially free of undissolved fentanyl.
2. (Original) The composition of claim 1 wherein the A monomer is selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate.
3. (Original) The composition of claim 1 wherein the A monomer is isooctyl acrylate.
4. (Original) The composition of claim 1 wherein the B monomer is selected from the group consisting of 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, glyceryl acrylate, N,N-diethylacrylamide, 2-ethoxyethoxyethyl acrylate, 2-ethoxyethyl acrylate, tetrahydrofurfuryl acrylate, acrylic acid, acrylamide, vinyl acetate, N-vinyl pyrrolidone and mixtures thereof.
5. (Original) The composition of claim 1 wherein the B monomer is 2-hydroxyethyl acrylate.

6. (Original) The composition of claim 5 wherein the copolymer comprises from about 5% to about 45% of 2-hydroxyethyl acrylate by weight based on the total weight of all monomers in the copolymer.

7. (Original) The composition of claim 1 wherein the copolymer further comprises a macromonomer.

8. (Original) The composition of claim 7 wherein the macromonomer is a functionally terminated polymethylmethacrylate.

9. (Original) The composition of claim 7 wherein the copolymer contains from about 1% to about 6% of macromonomer by weight based on the total weight of all monomers in the copolymer.

10-15. (Canceled).

16. (Original) The composition of claim 1 wherein the concentration of fentanyl in said transdermal drug delivery composition is from about 12% to about 24% by weight.

17. (Original) The composition of claim 7 wherein the copolymer comprises from about 50 to about 94% isooctyl acrylate, about 5% to about 40% 2-hydroxyethyl acrylate, about 1% to about 6% macromonomer, and 0% to about 20% vinyl acetate by weight.

18. (Original) The composition of claim 7 wherein the copolymer comprises from about 52% to about 60% isooctyl acrylate, about 35% to about 40% 2-hydroxyethyl acrylate, about 1% to about 4% macromonomer, and 0% to about 10% vinyl acetate by weight.

19-27. (Canceled).

28. (Original) A method of treating in a mammal a condition capable of treatment by fentanyl comprising the steps of:

- (a) providing a composition according to claim 1;
- (b) placing the composition on the skin of a mammal; and
- (c) allowing the composition to remain on the skin for a time sufficient to establish or maintain a therapeutically effective blood level of fentanyl in the mammal.

29. (Original) A method of providing analgesia to a mammal comprising the steps of:

- (a) providing a composition according to claim 1;
- (b) placing the composition on the skin of a mammal; and
- (c) placing the composition to remain on the skin for a time sufficient to establish or maintain an analgesically effective blood level of fentanyl in the mammal.

30. (Previously presented) A method of providing sustained analgesia to a mammal comprising delivering fentanyl to a mammal via a transdermal drug delivery device in an amount of about 0.5 to about 5.0 mg/day thereby causing the serum concentration of fentanyl in the mammal to be about 0.2 to about 10 ng/mL for a period of time from about 4 to about 14 days, wherein the device includes a composition according to claim 1.

31. (Original) The method of claim 30 wherein the fentanyl is delivered in an amount of 0.5 to 2.5 mg/day, the serum concentration of fentanyl in the mammal is about 0.3 to about 4 ng/mL, and the period of time is from about 6 to about 8 days.

32-34. (Canceled).

35. (Currently amended) A transdermal drug delivery composition ~~consisting of~~ comprising:

- (a) a copolymer comprising:
  - (i) one or more A monomers selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate; and

(ii) one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; wherein the B monomers are selected from the group consisting of 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, glyceryl acrylate, N,N-diethylacrylamide, 2-ethoxyethoxyethyl acrylate, 2-ethoxyethyl acrylate, tetrahydrofurfuryl acrylate, acrylic acid, acrylamide, vinyl acetate, N-vinyl pyrrolidone and mixtures thereof; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition;

wherein the composition is substantially free of undissolved fentanyl.

36. (Currently amended) A transdermal drug delivery composition ~~consisting of~~ comprising:

(a) a copolymer comprising:

(i) one or more A monomers selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate; and

(ii) about 5% to about 45% of one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; wherein the B monomers are selected from the group consisting of 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, glyceryl acrylate, N,N-diethylacrylamide, 2-ethoxyethoxyethyl acrylate, 2-ethoxyethyl acrylate, tetrahydrofurfuryl acrylate, acrylic acid, acrylamide, vinyl acetate, N-vinyl pyrrolidone and mixtures thereof; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition;

wherein the composition is substantially free of undissolved fentanyl.

37. (Currently amended) A transdermal drug delivery composition ~~consisting of~~ comprising:

(a) a copolymer comprising

(i) one or more A monomers selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate; and

(ii) about 5% to about 45% of one or more ethylenically unsaturated B monomers copolymerizable with the A monomer, wherein at least one B monomer is 2-hydroxyethyl acrylate; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition;

wherein the composition is substantially free of undissolved fentanyl; and wherein the drug delivery device delivers fentanyl to a mammal via a transdermal drug delivery device in an amount of about 0.5 to about 5.0 mg/day thereby causing the serum concentration of fentanyl in the mammal to be about 0.2 to about 10 ng/mL for a period of time from about 4 to about 14 days.

38. (Canceled).

39. (New). The composition of claim 1 wherein the composition further comprises a delivery enhancing adjuvant.

40. (New). The composition of claim 39 wherein the delivery enhancing adjuvant is selected from the group consisting of alkane polyols, fatty acids, fatty acid esters, fatty alcohols, terpenes, C<sub>5</sub>-C<sub>18</sub> alkyl esters of a carboxylic acid, and mixtures thereof.

41. (New). The composition of claim 39 wherein the delivery enhancing adjuvant is selected from the group consisting of ethyl oleate, isopropyl myristate, glycerol, tetraglycol, methyl laurate, N,N-dimethyldodecylamine N-oxide, limonene, terpineol, tetraethylene glycol, menthol, and mixtures thereof.

42. (New). The composition of claim 39 wherein the concentration of the delivery enhancing adjuvant is from about 5% to about 40% by weight based on the total weight of the composition.

43. (New). The composition of claim 39 wherein the skin permeation enhancer is tetraglycol.

44. (New). The composition of claim 39 wherein the skin permeation enhancer is methyl laurate.

45. (New). The composition of claim 17 wherein the concentration of fentanyl is from about 12% to about 22% by weight, wherein the composition further comprises about 15% to about 35% by weight of a permeation enhancer selected from the group consisting of methyl laurate, tetraglycol, and mixtures thereof.

46. (New). The composition of claim 45 wherein the concentration of fentanyl is from about 12% to about 17% by weight and the concentration of methyl laurate is from about 20% to about 35% by weight.

47. (New). The composition of claim 45 wherein the concentration of fentanyl is from about 15% to about 22% by weight and the concentration of tetraglycol is from about 15% to about 25% by weight.

48. (New). A pressure sensitive adhesive composition for the transdermal delivery of fentanyl comprising

- (a) an acrylate polymer;
  - (b) about 8% to about 30% by weight fentanyl based on the total weight of the composition; and
  - (c) a delivery enhancing adjuvant selected from the group consisting of methyl laurate, tetraglycol, and mixtures thereof;
- wherein the composition is substantially free of undissolved fentanyl.

49. (New). The composition of claim 48 wherein the concentration of delivery enhancing adjuvant is from about 5% to about 40% by weight based on the total weight of the composition.

50. (New). The composition of claim 48 wherein the acrylate polymer comprises:

(a) one or more A monomers selected from the group consisting of alkyl acrylates containing 4 to 12 carbon atoms in the alkyl group and alkyl methacrylates containing 4 to 12 carbon atoms in the alkyl group; and

(b) one or more ethylenically unsaturated B monomers copolymerizable with the A monomer.

51. (New). The composition of claim 50 wherein the B monomer is selected from the group consisting of 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, glyceryl acrylate, N,N-diethyacrylamide, 2-ethoxyethoxyethyl acrylate, 2-ethoxyethyl acrylate, tetrahydrofurfuryl acrylate, N-vinyl pyrrolidone and mixtures thereof.

52. (New). A device for the transdermal delivery of fentanyl comprising a backing and a composition according to claim 1, said composition being adhered to one surface of the backing.

53. (New). The composition of claim 39 wherein the delivery enhancing adjuvant is a skin permeation enhancer.

54. (New). A transdermal drug delivery composition comprising

(a) a copolymer comprising

(i) one or more A monomers selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate; and

(ii) about 5% to about 45% of one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; wherein at least one B monomer is 2-hydroxyethyl acrylate; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition; and

(c) a delivery enhancing adjuvant selected from the group consisting of methyl laurate, tetraglycol, and mixtures thereof;

wherein the composition is substantially free of undissolved fentanyl.

55. (New) A transdermal patch for administering fentanyl through the skin comprising: (a) a backing layer; (b) a reservoir disposed on the backing layer, at least the skin contacting surface of said reservoir being adhesive; said reservoir comprising a single phase polymeric composition free of undissolved components containing an amount of fentanyl sufficient to induce and maintain analgesia in a human for at least three days.

56. (New) The patch of claim 55 which is bioequivalent to DURAGESIC® transdermal fentanyl system.

57. (New) The patch of claim 55 wherein said reservoir is formed from an adhesive.

58. (New) The patch of claim 55 or 57 wherein said patch exhibits a normalized  $C_{\max}$  of about 16.8 to 18.7 ng/mL-mg/hr.

59. (New) The patch of claim 55 or 57 wherein said patch exhibits a standardized  $C_{\max}$  of about 0.14 to about 0.17 ng/mL/cm<sup>2</sup>.

60. (New) The patch of claim 57 wherein the patch exhibits a steady state drug flux of about 8.2 to 8.9 µg/cm<sup>2</sup>/hr.

61. (New) The patch of claim 55 wherein said reservoir comprises an amount of dissolved fentanyl sufficient to induce and maintain analgesia for about 4-14 days.

62. (New) The patch of claim 55 wherein said reservoir comprises an amount of dissolved fentanyl sufficient to induce and maintain analgesia for about 6-8 days.

63. (New) The patch of claim 55 wherein fentanyl has a solubility of about 8-30% by weight.



64. (New) The patch of claim 55 wherein fentanyl has a solubility of about 12-24% by weight.

65. (New) The patch of claim 61 wherein the reservoir comprises about 0.84 to 3.56 mg/cm<sup>2</sup> of fentanyl base.

66. (New) The patch of claim 65 wherein the reservoir comprises about 0.84 to 1.72 mg/cm<sup>2</sup> of fentanyl base.

67. (New) The patch of claim 61 wherein the reservoir has a dry coating weight of about 10 to 12 mg/cm<sup>2</sup>.

68. (New) The patch of claim 57 wherein said adhesive is a polyacrylate adhesive.

69. (New) The patch of claim 68 wherein said polyacrylate adhesive has a T<sub>g</sub> less than -10° C.

70. (New) The patch of claim 68 wherein the reservoir comprises about 0.84 to 3.56 mg/cm<sup>2</sup> of fentanyl base.

71. (New) The patch of claim 70 wherein the reservoir comprises about 0.84 to 1.72 mg/cm<sup>2</sup> of fentanyl base.

72. (New) The patch of claim 68 wherein the reservoir has a dry coating weight of about 10 to 12 mg/cm<sup>2</sup>.

73. (New) The patch of claim 61 or claim 68 wherein the reservoir further comprises an enhancer.

74. (New) The patch of any one of claims 55, 61 or 68, wherein the backing layer comprises a polymer selected from the group consisting of polyethylene, polyethylene terephthalate, ethylene-vinyl acetate copolymer, and polyurethane.

75. (New) The patch of claim 74, wherein the backing layer comprises low density polyethylene or high density polyethylene.

76. (New) The patch of claim 75, wherein the backing layer comprises low density polyethylene.

77. (New) The patch of claim 74 wherein the backing layer has a thickness of about 0.05 mm.

78. (New) A transdermal patch for administering fentanyl, comprising an adhesive fentanyl reservoir on a backing layer; said reservoir comprising a single phase polymeric composition free of undissolved components containing a polyacrylate adhesive having sufficient solubility for fentanyl to contain dissolved fentanyl in an amount sufficient to induce and maintain analgesia in a human for at least three days, said patch exhibiting a normalized  $C_{\max}$  of about 16.8 to 18.7 ng/mL-mg/hr.

79. (New) A transdermal patch for administering fentanyl, comprising an adhesive fentanyl reservoir on a backing layer; said reservoir comprising a single phase polymeric composition free of undissolved components containing a polyacrylate adhesive having sufficient solubility for fentanyl to contain dissolved fentanyl in an amount sufficient to induce and maintain analgesia in a human for at least three days, said patch exhibiting a standardized  $C_{\max}$  of about 0.14 to about 0.17 ng/mL/cm<sup>2</sup>.

80. (New) The patch of claim 78 or 79 wherein the patch exhibits a steady state drug flux of about 8.2 to 8.9  $\mu\text{g}/\text{cm}^2/\text{hr}$ .

81. (New) The patch of claim 78 or 79 wherein said reservoir comprises an amount of dissolved fentanyl sufficient to induce and maintain analgesia for about 4-14 days.

82. (New) The patch of claim 78 or 79 wherein said reservoir comprises an amount of dissolved fentanyl sufficient to induce and maintain analgesia for about 6-8 days.

83. (New) The patch of claim 81 wherein said adhesive is a polyacrylate adhesive having a  $T_g$  less than  $-10^\circ\text{C}$ ; and fentanyl has a solubility of about 8% by weight.

84. (New) The patch of claim 83 wherein the reservoir has a dry coating weight of about 10 to 12  $\text{mg}/\text{cm}^2$ .

85. (New) The patch of claim 84 wherein the reservoir comprises about 0.84 to 3.56  $\text{mg}/\text{cm}^2$  of fentanyl base.

86. (New) The patch of claim 85 wherein the reservoir comprises about 0.84 to 1.72  $\text{mg}/\text{cm}^2$  of fentanyl base.

87. (New) A monolithic transdermal patch for administering fentanyl, comprising an adhesive fentanyl reservoir on a backing layer, said reservoir comprising a single phase polymeric composition free of undissolved components containing a polyacrylate adhesive having sufficient solubility for fentanyl to contain dissolved fentanyl in an amount sufficient to induce and maintain analgesia in a human for at least three days, said patch being completely free from a rate controlling membrane, said patch exhibiting a normalized  $C_{\text{max}}$  of about 16.8 to 18.7  $\text{ng}/\text{mL}\text{-mg}/\text{hr}$ .

88. (New) A monolithic transdermal patch for administering fentanyl, comprising an adhesive fentanyl reservoir on a backing layer, said reservoir comprising a single phase polymeric composition free of undissolved components containing a polyacrylate adhesive

having sufficient solubility for fentanyl to contain dissolved fentanyl in an amount sufficient to induce and maintain analgesia in a human for at least three days, said patch being completely free from a rate controlling membrane, said patch exhibiting a standardized  $C_{\max}$  of about 0.14 to about 0.17 ng/mL/cm<sup>2</sup>.

89. (New) The patch of claim 87 or 88 wherein said reservoir comprises an amount of dissolved fentanyl sufficient to induce and maintain analgesia for about 6-8 days wherein fentanyl has a solubility of about 8% by weight in said reservoir; the reservoir has a drying coating weight of about 10-12 mg/cm<sup>2</sup>; and said patch exhibits a steady state drug flux of about 8.2 to 8.9 µg/cm<sup>2</sup>/hr.

90. (New) The patch of claim 87 or 88 wherein the reservoir comprises about 0.84 to 3.56 mg/cm<sup>2</sup> of fentanyl base.

91. (New) The patch of claim 55 which is pharmacologically equivalent to DURAGESIC® transdermal fentanyl system.